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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/308,218	09/19/1994	MARC ALIZON	3495.001019	4831

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 12/20/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/308,218	Applicant(s) ALIZON ET AL.	
	Examiner Jeffrey Fredman	Art Unit 1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Double Patenting

The double patenting rejections are withdrawn in view of the amendment.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 26 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

Claim 26 encompasses a genus of nucleic acids which are different from the single species disclosed in the specification. The genus includes variants for which no written description is provided in the specification. Thus, applicant has express

possession of only one particular nucleic acid sequence which might encode a protein which could bind a Nef specific antibody, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the nucleic acid as encoding something which can be bound by an antibody lacks any specific structure and is precisely the situation of naming a type of material which is generally known to likely exist, but, except for the specific sequence, is in the absence of knowledge of the material composition.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a deletion, without any definition of the particular deletions claimed.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than that expressly disclosed. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Claims 14-29 are rejected under 35 U.S.C. 102(e) as being anticipated by Chang et al (U.S. Patent 6,001,977).

Chang teaches nucleic acid probes of HIV-1 selected from the HIV sequence (column 9, lines 25-62 and column 10, line 65 to column 11, line 32), where the specific sequence is disclosed as SEQ ID NO: 4, for example (columns 19-28).

Chang further teaches the compositions of these nucleic acids (column 9, lines 25-62) as well as HTLV-I and II negative control sequences (column 9, lines 25-62).

Chang expressly teaches formation of expression vectors, including an E. coli expression library which would contain every open reading frame (see column 5, line 66 to column 6, line 12).

Chang expressly teaches mammalian and yeast vectors (see column 6, lines 9-13).

Chang further teaches the compositions of these nucleic acids (column 9, lines 25-62) as well as HTLV-I and II negative control sequences (column 9, lines 25-62).

Chang teaches methods of expression and making recombinant DNA molecules (see columns 5 and 6).

The alignment of the Query HIV sequences of Chang and the subject sequences of the present application in the region between nucleotides claimed are presented below.

```
Query:                                      gacagggcttggaaaggattttgctataaga 8153
                                            ||||||||||||||||||||||||||||||
Sbjct:                                      gacagggcttggaaaggattttgctataaga 8354
orfF   1                                     D  R  A  W  K  G  F  C  Y  K
env    851    A  I  R  H  I  P  R  R  I  R  Q  G  L  E  R  I  L  L ^^^


Query: 8154 tgggtggcaagtggtcaaaaagtagtgtggttggatggcctgctgtaagggaaagaatga 8213
             |||||||||||||||||||||||||||||||||||||||||||||| ||||||||||||||||||
Sbjct: 8355 tgggtggcaagtggtcaaaaagtagtgtggttggatggcctactgtaagggaaagaatga 8414
orfF   11   M  G  G  K  W  S  K  S  S  V  V  G  W  P  T  V  R  E  R  M


Query: 8214 gacgagctgagccagcagcagatggggtgggagcagcatctcgagacctagaaaaacatg 8273
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||| ||||||||||
Sbjct: 8415 gacgagctgagccagcagcagatggggtgggagcagcatctcgagacctggaaaaacatg 8474
orfF   31   R  R  A  E  P  A  A  D  G  V  G  A  A  S  R  D  L  E  K  H


Query: 8274 gagcaatcacaagtagcaacacagcagctaacaatgctgattgtgcctggctagaagcac 8333
             |||||||||||||||||| |||||||||| |||||||| ||||||||||||||||||||
Sbjct: 8475 gagcaatcacaagtagcaatacagcagctaccaatgctgcttgtgcctggctagaagcac 8534
orfF   51   G  A  I  T  S  S  N  T  A  A  T  N  A  A  C  A  W  L  E  A


Query: 8334 aagaggaggaggaggtgggttttccagtcacacctcaggtacctttaagaccaatgactt 8393
             |||||||||||||||||||||||| ||||||||||||||||||||||||||||||||||
Sbjct: 8535 aagaggaggaggaggtgggttttccactcacacctcaggtacctttaagaccaatgactt 8594
orfF   71   Q  E  E  E  E  V  G  F  P  L  T  P  Q  V  P  L  R  P  M  T
```

```
Query: 8394 acaaggcagctgtagatcttagccacttttaaaagaaaaggggggactggaagggctaa 8453
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 8595 acaaggcagctgtagatcttagccacttttaaaagaaaaggggggactggaagggctaa 8654
orfF   91   Y  K  A  A  V  D  L  S  H  F  L  K  E  K  G  G  L  E  G  L

Query: 8454 ttcactcccaacgaagacaagatatccttgatctgtggatctaccacacacaaggctact 8513
            ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Sbjct: 8655 ttcactcccaacgaagacaagatatccttgatctgtggatctaccacacacaaggctact 8714
orfF   111  I  H  S  Q  R  R  Q  D  I  L  D  L  W  I  Y  H  T  Q  G  Y

Query: 8514 tccctgattagcagaactacacaccagggccagggatcagatatccactgacctttggat 8573
            |||||||||  ||||||||||||||||||||||||  ||||||||||||||||||||||
Sbjct: 8715 tccctgattggcagaactacacaccagggccaggggtcagatatccactgacctttggat 8774
orfF   131  F  P  D  W  Q  N  Y  T  P  G  P  G  V  R  Y  P  L  T  F  G

Query: 8574 ggtgctacaagctagtaccagttgagccagagaagttagaagaagccaacaaaggagaga 8633
            |||||||||||||||||||||||||||||  |||  |||||||  |||||  ||||||||||
Sbjct: 8775 ggtgctacaagctagtaccagttgagccagataaggtagaagaggccaataaaggagaga 8834
orfF   151  W  C  Y  K  L  V  P  V  E  P  D  K  V  E  E  A  N  K  G  E

Query: 8634 acaccagcttgttacaccctgtgagcctgcatggaatggatgacccggagagagaagtgt 8693
            ||||||||||||||||||||||||||||||||||||||||||||||  ||||||||||||
Sbjct: 8835 acaccagcttgttacaccctgtgagcctgcatggaatggatgaccctgagagagaagtgt 8894
orfF   171  N  T  S  L  L  H  P  V  S  L  H  G  M  D  D  P  E  R  E  V

Query: 8694 tagagtggaggtttgacagccgcctagcatttcatcacatggcccgagagctgcatccgg 8753
            ||||||||||||||||||||||||||||||||||||  ||||||||||||||||||||||
Sbjct: 8895 tagagtggaggtttgacagccgcctagcatttcatcacgtggcccgagagctgcatccgg 8954
orfF   191  L  E  W  R  F  D  S  R  L  A  F  H  H  V  A  R  E  L  H  P

Query: 8754 agtacttcaagaactgc
            |||||||||||||||||
Sbjct: 8955 agtacttcaagaactgc
orfF   211  E  Y  F  K  N  C ^^^
```

It is noted that with regard to, for example, the sequence region between shown above, there are 14 nucleotide differences between the sequences, yielding about a 2% error rate. It is noted that the art recognizes that sequencing errors occur in a range between 0.3 % and 2.5%, as evidenced by Richterich (Genome Research (1998) 8:251-259). However, these error rates are determined using technology that was

significantly more advanced than that in 1984, when sequencing error rates were likely significantly higher. Thus, these sequences are identical within the error range available and the anticipation rejection is proper.

With regard to the kit claims, it is noted that the preamble phrase "a kit" imposes no structural requirements upon the product claims.

Response to Arguments

3. Applicant's arguments filed November 18, 2002 have been fully considered but they are not persuasive.

Applicant argues that a comparison of the sequences of Chang and the present case show that Chang has stop codons which would prevent expression of the ORFs. This argument is not found persuasive for several reasons.

First, it is not simply the sequence which Chang teaches, but the specific DNA entity, the composition, which was in the lab. Because of the issue of sequencing error, addressed in the rejection itself, it is unclear whether these differences between the sequences identified by Applicant represent real differences or simply sequencing error. If the differences are real, as evidenced by a declaration (which is expressly invited), then applicant's argument would be persuasive. However, given the high probability of sequencing errors as discussed above, combined with the knowledge that due to contamination, the virus strain of Chang was the same virus strain as that used by Applicant, the rejections are maintained.

Second, since the claims are comprising, a diagnostic vector which comprises the entirety of the HIV genome would inherently comprise each and every ORF,

including those claimed. Since such a vector is within the teaching of Chang, this clearly anticipates the current claims.

Third, to the extent that the argument relies upon the fact that Chang did not correctly identify these open reading frames due to the presence of stop codons, this argument is not persuasive because formation of random fragments as taught by Chang will create the vectors irrespective of whether Chang was aware of the open reading frames or not.

Fourth, to the extent that the argument relies upon actual sequence differences which create different open reading frames, no evidence is on record showing that the sequences are, in fact, different. A declaration which evidenced such a difference in sequence, which directly corresponded to a claim, would be valuable in this application and applicant is expressly invited to provide such a declaration. Currently, there is no evidence which rebuts the position that any differences are the result of sequencing error.

As a final point, it is noted that in this case, there is better evidence than is ordinarily available that the strains sequenced by the two different groups are, in fact, the same since it is clear that the LAI strain is common to both of these applications.

Conclusion

4. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1637

December 19, 2002